Nanoparticle Delivery of TWIST Small Interfering RNA and Anticancer Drugs: A Therapeutic Approach for Combating Cancer.

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Public Summary:
Breast and ovarian cancer are the leading cause of cancer-related deaths in women in the United States with over 232,000 new Breast Cancer (BC) diagnoses expected in 2018 and almost 40,000 deaths and an estimated 239,000 new ovarian cancer (OC) cases and 152,000 deaths worldwide annually. OC is the most lethal gynecologic malignancy. This high mortality rate is due to tumor recurrence and metastasis, primarily caused by chemoresistant cancer stem-like cells (CSCs). Triple Negative Breast Cancer (TNBC) patients also become resistant to chemotherapy due to recurrence of CSCs. Currently, no ovarian or breast cancer therapies target CSC specifically. TWIST is overexpressed in the majority of chemoresistant cancers resulting in a low survival rate. Our long-term goal is to develop novel treatments for women with ovarian and breast cancer, specifically treatments that sensitize chemoresistant tumors. Despite successful initial surgery and chemotherapy, over 70% of advanced EOC will recur, and only 15-30% of recurrent disease will respond to chemotherapy (Cortez et al., 2017; Berezhnaya, 2010; Jackson et al., 2015). Moreover, drug resistance causes treatment failure in over 90% of patients with metastatic disease (Solmaz et al., 2015). Thus, recurrent metastatic disease is a major clinical challenge without effective therapy. One of the major challenges in the treatment of breast cancer is the presence of a subpopulation of cancer cells that are chemoresistant (CRC) and metastatic. Given that metastasis is the driving force behind mortality for breast and ovarian cancer patients, it is essential to identify the characteristics of these aberrant cancer cells that allow them to spread to distant sites in the body and develop into metastatic tumors. Understanding the metastatic mechanisms driving cancer cell dispersal will open the door to developing novel therapies that prevent metastasis and improve long-term outcomes for patients. In this chapter we assess the feasibility of targeting the Twist and EMT signaling pathways in breast and ovarian cancer. Additional discussions of the pathways that mediate epithelial-mesenchymal transition (EMT), a process that can give rise to chemoresistance. We review potential treatment strategies for targeting EMT and drug resistance as well as the problems that may arise with these targeted delivery therapeutic approaches. Finally, we examine recent advances in the field, including cancer stem cell targeted nanoparticle delivery and small interference RNA (siRNA) technology, and discuss the impact that these approaches may have on translating much needed therapeutic approaches into the clinic, for the benefit of patients battling this devastating disease.

Scientific Abstract:
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